Chapter 1

National Health and Nutrition Examination Survey (NHANES) III DNA Bank: Gene Variants Important to Public Health

Mary Lou Lindegren for the NHANES CDC-Wide Working Group

NHANES III DNA Bank

The National Health and Nutrition Examination Survey (NHANES) is a nationally representative survey of the United States population, conducted by the National Center for Health Statistics (NCHS).[1] Detailed interviews, clinical, laboratory and radiological examinations are conducted as part of the survey. NCHS has collected these data with an assurance of confidentiality.

During the second phase of NHANES III (1991-1994),[2] white blood cells were frozen and cell lines were immortalized with Epstein-Barr virus, creating a DNA bank.[3] The bank is maintained by the National Center for Environmental Health, CDC, and contains specimens from more than 7000 participants. In 2002, NCHS requested proposals for the use of these specimens.[4, 5]

Collaborative CDC-Wide Project

A CDC-wide working group of epidemiologists and laboratorians, representing most Centers and Institutes at CDC, was convened to develop a collaborative proposal for determining the prevalence of selected genotypes of public health importance using the NHANES III DNA Bank.

Selecting Genetic Variants Important to Public Health

The criteria used to select genes for the proposal included:

- known or hypothesized association with diseases of public health importance,
- role in pathways affecting multiple diseases,
- identified functional variants,
- relatively common variants (prevalence >2%),
- previously described gene-environment or gene-gene interactions,
- relevant phenotypic data available in NHANES datasets, and
- no current use for clinical risk assessment or intervention.

Several challenges that made this process difficult were:

- gaps in published information,
- many available studies demonstrated problems with methodology, including selection bias, small sample size, and lack of attention to potential interaction, and
- non-replication of many published gene-disease associations.

The final proposal included 87 variants of 57 genes known to be important in at least six major pathways:

- nutrient metabolism (e.g., folate and homocysteine; lipids; glucose; alcohol; vitamin D),
- immune and inflammatory responses (e.g., cytokines, cytokine receptors),
- activation and detoxification pathways (e.g., drugs, carcinogens, environmental contaminants),
- DNA repair pathways (e.g., ionizing radiation, environmental toxins),
- hemostasis and renin/angiotension pathways, and
- developmental pathways.

Genotyping will be performed in collaboration with the National Cancer Institute (NCI) at the NCI Core Genotyping Facility.

Potential Value for Public Health

Prevalence data from the NHANES database will be the basis for future analysis of gene-disease associations and gene-environment interactions. Gene-environment interactions are considered to be the fundamental biological processes that both maintain health and bring about disease. As our understanding of these interactions grows, establishing the prevalence of **gene variants** known to interact with specific environmental factors will be a key factor in assessing the potential impact of environmental interventions. Genotypic information will add another dimension to the analysis of clinical, physical, and lifestyle information collected by NHANES. Additional analysis of **genotype-phenotype** relations will be proposed once the prevalence data have been evaluated.

Prevalence
The number of people with a trait or condition at a specific point in time.

Gene Variant
A variation in the sequence most commonly observed for a particular gene.

Genotype
The genetic make-up of an individual.

Phenotype
The observable traits or characteristics of an individual.

Two Other CDC Projects Using NHANES III DNA Samples

Prevalence of Gene Variants that Code for Enzymes Involved in Nicotine and Carcinogen Metabolism in the United States Population and their Association with Body Burden of Cotinine

Karen Steinberg, et al.

This proposal involves correlating over 40 **Single Nucleotide Polymorphisms** or **SNPs** (pronounced "snips") in 14 genes involved in drug-nicotine metabolism and smoking behavior with serum cotinine measurements already performed, and with self-reported smoking variables.

Frequency of Common Genotypes of Folate-Related Genes and their Effect on the Relation between Intake and Blood Levels of Folate and Homocysteine

Lorenzo Botto, et al.

This proposal will evaluate the individual and joint effects (interactions) of selected common polymorphisms of three genes in the folate metabolism pathway and the consumption of folic acid on homocysteine and folate levels.

Single Nucleotide Polymorphism – SNP
Common, but minute, variations that occur in human DNA at a frequency of one in every 1,000 bases.

NHANES CDC-Wide Working Group
http://www.cdc.gov/genomics/NHANES.htm

ATSDR	Agency for Toxic Substances and Disease Registry
NCBDDD	National Center on Birth Defects and Developmental Disabilities
NCHSTP	National Center for HIV, STD, and TB Prevention
NCID	National Center for Infectious Diseases
NCEH	National Center for Environmental Health
NCCDPHP	National Center for Chronic Disease Prevention and Health Promotion
NIOSH	National Institute for Occupational Safety and Health
NIP	National Immunization Program
NCHS	National Center for Health Statistics
OGDP	Office of Genomics and Disease Prevention
PHPPO	Public Health Practice Program Office

References

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